

# Peutz-Jeghers polyp: A Retrospective Study on Twelve Cases Received at the Department of Pathology, Bangabandhu Sheikh Mujib Medical University

Tamanna Choudhury<sup>1</sup>, Suraiya Enam<sup>2</sup>, Ferdousy Begum<sup>3</sup>, Md. Taufiq<sup>4</sup>, Mohammed Kamal<sup>5</sup>

<sup>1</sup>Associate Professor, <sup>2</sup>Assistant Professor, <sup>3</sup>Associate Professor, Department of Pathology, Bangabandhu Sheikh Mujib Medical University, <sup>4</sup>Lecturer, Department of Cytopathology, National Institute of Cancer Research and Hospital (NICRH), Dhaka, <sup>5</sup>Chairman and Professor, Department of Pathology, Bangabandhu Sheikh Mujib Medical University

## Abstract:

**Background:** Peutz Jegher syndrome is a rare inherited condition characterized mainly by gastrointestinal hamartomatous polyposis and mucocutaneous pigmentation. The polyps are mostly found in the small bowel and less frequently in the stomach and large gut. **Objectives:** This study was done to observe the clinical and pathological features of Peutz Jegher polyps. **Methods:** A retrospective study was carried out in the Department of Pathology, Bangabandhu Sheikh Mujib Medical University (BSMMU) during the five and a half year period from 1<sup>st</sup> January 2006 to 30<sup>th</sup> June 2011. From the records the cases which were diagnosed as Peutz Jeghers polyps were sorted out, clinical data was compiled and slides were reviewed. **Results:** During this period 12 cases were diagnosed as Peutz Jeghers polyp. Most of these (n=58.33%) occurred in the second decade of life and majority (n=9) were located in the large gut including sigmoid colon and rectum. Both sessile as well as pedunculated types were seen. All had characteristic histologic features of Peutz Jeghers polyps and in only one case there was a mild dysplastic change in the glandular lining epithelium. **Conclusion:** Close monitoring of the patients with peutz Jeghers polyp can reduce the morbidity of this condition.

**Keywords:** *Peutz Jeghers syndrome, Hamartomatous polyp, Mucocutaneous pigmentation*

[BSMMU J 2012; 5(1):12-17]

## Introduction:

Peutz Jegher syndrome (PJS) is an inherited cancer syndrome with autosomal dominant trait,<sup>1</sup> characterized by mucocutaneous melanin pigmentation and hamartomatous intestinal polyposis preferentially affecting the small intestine.<sup>1-4</sup> Most patients have a characteristic clinical course of recurrent episodes of polyp induced bowel obstruction. PJS is a rare disease<sup>1,5,6</sup>. Well documented data on the incidence are not available<sup>1</sup> and according to a study, the estimated incidence is 1 in 300,000 births.<sup>7</sup>

In addition to polyposis, the risk of gastrointestinal and extra intestinal malignancies is significantly increased in PJS patients.<sup>1-4,8</sup> We carried out a retrospective study in the Department of Pathology, Bangabandhu Sheikh Mujib Medical University to observe the clinical and pathological features of PJS polyps for a period of five and a half years.

## Methods:

In this retrospective study records of the surgical specimens received in the Department of Pathology, Bangabandhu Sheikh Mujib Medical University (BSMMU) during the five and a half years period from 1<sup>st</sup> January

2006 to 30<sup>th</sup> June 2011 were reviewed. From these records, the cases which were diagnosed as Peutz Jeghers polyps were sorted out, clinical data was compiled and slides were reviewed. Fresh sections were made from paraffin blocks. All the sections were stained with heamatoxylin and eosin methods. Masson's trichrome stain was used in selected cases.

## Results:

Out of a total of 44,615 surgical pathology specimens during this five and a half years period, 46 polypoid lesions were diagnosed in the gastrointestinal tract. Of these, 12 cases were diagnosed as Peutz Jeghers polyp. Out of 12 patients, nine were male and three were female.

In this study group, the age range was from 15 to 52 year with a mean age of 27.75 year. Majority (58.33%) were in the second decade of life. Table I shows the age distribution of the patients.

Relevant clinical information was available in 4 cases only. Three of these patients presented with mucocutaneous pigmentation in the lip (Fig 1), peri-oral skin and buccal mucosa and also had history of per rectal bleeding. History of malena was present in two patients out of four and only one patient had the complaint of abdominal pain.

Information regarding family history was available in three cases only and all of them had family history of similar manifestations in other members of the family.

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**Address for Correspondence:** Dr. Tamanna Choudhury, Associate Professor, Department of Pathology, Bangabandhu Sheikh Mujib Medical University, Dhaka

**Table-I**  
*Age distribution*

Age in years	Number of patients (n=12)	Percentage (%)
<10	00	001
1-20	07	58.33
21-30	01	8.33
31-40	01	8.33
41-50	02	16.67
51-60	01	8.33
>61	00	00

**Table-II**

*Anatomic distribution of polyps with nature of surgery*

Anatomic location with nature of surgery	Number (n=12)	Percentage (%)
Large gut (resected)	04	33.33
Rectum (polypectomy)	03	25
Sigmoid colon (polypectomy)	02	16.66
Stomach (polypectomy)	01	8.33
Duodenum (polypectomy)	01	8.33
Duodenum, jejunum, ileum (polypectomy)	01	8.33

Records of endoscopic/colonoscopic findings were available in five patients. Multiple polyps (Fig 2) were present in all five (100%) patients.



**Fig.- 1:** *Mucocutaneous pigmentation in the lower lip (arrow)*



**Fig.-2:** *Multiple polyps of different sizes and shapes seen scattered throughout the whole colon- starting from lower rectum up to caecum*

Out of twelve, eight were polypectomy specimen and 4 were resected specimen. In cases of polypectomy, polyps were removed from rectum (3 cases), sigmoid colon (2 cases), one case each from duodenum and stomach. In one case multiple polyps were removed separately from duodenum, jejunum and ileum. Resected specimens (4 cases) were all from the colon. Majority (n=74.99%) of polyps were in the large gut including sigmoid colon and rectum, followed by polyps in the stomach and small intestine including duodenum, jejunum and ileum (24.99%). (Table II).

Grossly, the sizes of the polyps ranged from 1.8 cm to 4.5 cm. and cut surfaces were solid and grayish white in colour. In resected specimens, the number of polyps ranged from seven up to numerous (Fig 3, 4). Both sessile as well as pedunculated polyps were found.

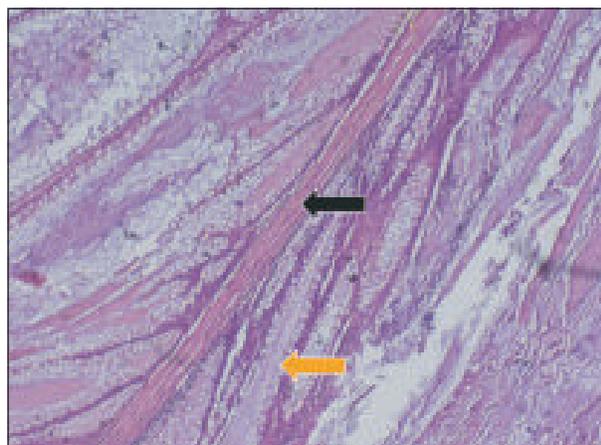


**Fig.-3:** *Colon showing multiple polyps (arrows)*



**Fig.-4:** Colon showing multiple polyps (arrows)

Microscopically, all the polyps had arborizing network of connective tissues and smooth muscle extending through the core of the polyp surrounded by intestinal glands lined by normal intestinal epithelium (Fig 5, 6). Masson's



**Fig.-5:** Microscopic section of a polyp showing muscular framework (black arrow) and glandular lining (orange arrow) (H&E X 200)

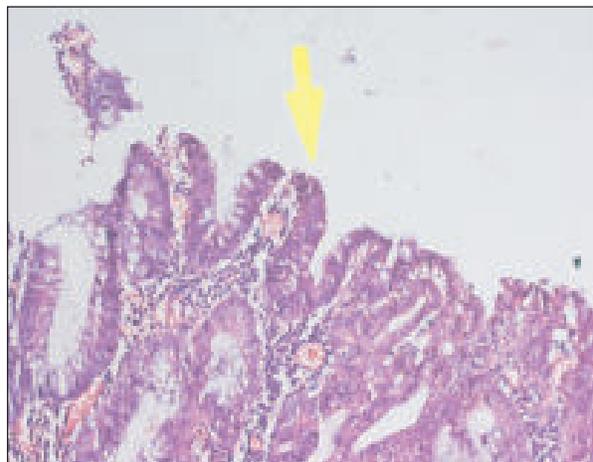


**Fig.-6:** Microscopic section of a polyp showing arborizing muscular framework (black arrows) (H&E X 200)

trichrome stain demonstrated the presence of diagnostic central core of smooth muscle (Fig.-7) within the polyp. Dysplasia of the glandular lining epithelium was seen in one case only (Fig.-8).



**Fig.-7:** Section of a polyp with diagnostic central core of smooth muscle (red stain) (Masson trichrome X 200)



**Fig.-8:** Microscopic section of the polyp showing dysplastic changes in the lining epithelium (arrow) (H&E X 100)

#### Discussion:

Peutz Jeghers syndrome is a rare familial disease first described by Peutz in 1921 and Jeghers in 1949 as cited by Aaltonen et. al<sup>1</sup> and Sökmen et. al.<sup>9</sup> This rare autosomal dominant disorder presents with multiple gastrointestinal hamartomatous polyps and mucocutaneous hyperpigmentation.<sup>3,5,9</sup> In our series, out of 44,615 surgical specimens in a period of five and a half year, only 12 cases were diagnosed as PJS polyp out of total 46 gastrointestinal polyps. The average age at PJS diagnosis is 23 year in men and 26 year in women.<sup>7</sup> The mean age in our series

was 27.75 year. The disease affects males and females equally<sup>5,7</sup>. But in our series males were more (75%) in number than the females. PJS has been described in all races.<sup>7</sup>

The following criteria are used to diagnose Peutz Jeghers polyp (i) three or more histologically confirmed Peutz Jeghers polyps, or (ii) any number of Peutz Jeghers polyps with a family history of PJS, or (iii) characteristic prominent mucocutaneous pigmentation with a family history of PJS, or (iv) any number of Peutz Jeghers polyps and characteristic prominent mucocutaneous pigmentation<sup>1,2,10</sup>.

Approximately 50% of cases are familial and 50% are sporadic with new mutations<sup>2</sup>. Germline heterozygous loss of function mutations in the gene LKB1/ serine threonine kinase (STK11) are present in 50% of individuals with familial PJS and in a subset of patients with sporadic PJS<sup>3</sup>. STK11 gene is located in chromosome 19p13.3.<sup>1,2,11,12</sup>

Most patients present with abdominal pain, intestinal bleeding, anaemia, and intussusception<sup>1</sup> mucosal pigmentation and intestinal polyposis.<sup>5,9</sup> In our study, clinical information was available only in four out of total twelve cases. Mucosal pigmentation was present in three cases; located in the lips, perioral areas and buccal mucosa. The hyperpigmentation emerges in the infancy or in childhood and consists of greenish black to brown melanin deposits on the lips, buccal mucosa, periorbital area, nose, hands, feet and occasionally the genital and perianal skin.<sup>1,2,7,12</sup> Pigmented lesions may fade at puberty, except for lesions on the buccal mucosa, making the diagnosis possible in pediatric patients with a high level of suspicion.<sup>7</sup>

Polyps may occasionally be absent<sup>5</sup> and conversely some patients have only intestinal polyps.<sup>2</sup> Most patients develop gastrointestinal symptoms during adolescence and young adulthood. Diffuse gastrointestinal polyposis causes intussusceptions<sup>8,13,14</sup> or obstruction presenting as recurrent attacks of crampy abdominal pain.<sup>2,6</sup> Intestinal polyps also can cause iron deficiency anaemia by producing overt or occult bleeding into the gastrointestinal lumen.<sup>9,15</sup> In our study three patients had per rectal bleeding and two patients had history of melena.

Grossly, the polyps of PJS arise throughout the gastrointestinal tract to affect the jejunum, ileum, colon, stomach, duodenum and appendix in decreasing order of frequency<sup>2</sup>. Rare polyps develop in the oesophagus, nasopharynx, urinary tract and gallbladder.<sup>1,2,9</sup> Gastric PJS polyps occur less commonly in western population

than in the Japanese.<sup>16</sup> In our study, majority (n=74.99%) of polyps were in the large gut including sigmoid colon and rectum, followed by polyps in the stomach and small intestine together constituting 24.99%. Though PJS polyps occur mostly in small intestine, the pathologists should be aware and careful while microscopically evaluating large gut polyps. Intestinal polyps usually number in dozens. Jejunal polyps can reach up to 100 in number.<sup>9</sup> In the resected specimens of our present study we observed variable numbers of polyps ranging from seven to numerous polyps. PJS polyps can be sessile as well as pedunculated<sup>17</sup> and we also observed both sessile as well as pedunculated polyps in our study. They range in size from few mm to over 7 cm; most measures 0.5 to 3.0 cm in diameter.<sup>2,5</sup> In this present series, the size range of the polyps was from 1.8 to 4.5cm in diameter.

Microscopically, PJS polyps have a distinctive histological appearance. A typical Peutz-Jeghers polyp has a diagnostically useful central core of smooth muscle that shows tree-like

branching<sup>1</sup> becoming progressively thinner as they reach the polyp surface.<sup>2</sup> This is covered by the mucosa native to the region, heaped into folds producing a villous pattern<sup>1</sup>. In our study all the polyps revealed these distinctive histologic features. During histopathology evaluation, a mistaken diagnosis of cancer can be made if dysplastic epithelium is located in the submucosa and muscularis mucosa.<sup>18</sup> In our study, features of dysplastic changes in the lining epithelium were present in one case only. It is thought that intestinal cancers seen in PJS patients may have originated in the polyp's epithelium and it is therefore essential that every polyp is excised and examined.

Epithelial misplacement involving all layers of the bowel wall (pseudoinvasion) has been described in up to 10% of small intestinal Peutz-Jeghers polyps.<sup>1</sup> Epithelial misplacement may be florid and extend into the serosa, thereby mimicking a well differentiated adenocarcinoma. Useful diagnostic features are the lack of cytological atypia, presence of all the normal cell types, mucinous cysts and haemosiderin deposition.<sup>1</sup> PJS polyps may be confused with adenomas which may also contain bands of smooth muscle fibres, but well demarcated focus of dysplasia favours adenoma. Juvenile polyps do not have smooth muscles and have expanded lamina propria. Inflammatory polyp may be mistaken as PJS polyp but the glands are haphazardly arranged.<sup>2</sup>

Polyps should be removed because they are prone to mechanical injury and they may contain areas of dysplasia or invasive cancer.<sup>2</sup> Patients with this syndrome have a high risk of gastrointestinal or extra gastrointestinal

malignancy including gastric, duodenal, jejunal, ileal, and colonic carcinoma as well as malignancies involving other organs such as the gallbladder, biliary tract, pancreas, tonsils, breast, lungs, ovaries, uterus and testis.<sup>1-3, 8</sup> There are well documented reports of carcinoma arising in PJS and in some cases associated adenomatous or dysplastic changes are observed within hamartomatous polyp.<sup>19-22</sup> Unusual adenoma malignum of uterine cervix has also been documented to be associated with PJS polyps.<sup>23</sup>

The cancer risk is 15 times greater for patients with PJS than for general population.<sup>2, 20, 24</sup>

Because of the increased risk for cancer, it is recommended that patients should undergo screening. One should be screened for PJS if a family history of PJS or any intestinal cancer at a young age, or any unusual symptoms (per rectal bleeding, abdominal pain etc). An initial screening should be done by 10-12 years of age or at the time of first symptom.<sup>25</sup> Screening recommended for gastrointestinal (GI) malignancies include upper GI endoscopy/ colonoscopy beginning with symptoms or in the late teens if no symptoms occur.<sup>2</sup> Screening for pancreatic cancer involving endoscopic and abdominal USG every 1 to 2 years after the age of 30<sup>2</sup> and also serum CA19-9<sup>26</sup> Screening for breast cancer involves annual breast examination and mammogram every 2 to 3 years beginning at age of 25. Screenings for gynaecologic neoplasm include annual pelvic examination with Pap smear beginning around the age of 20 years<sup>2</sup> and serum CA-125.<sup>26</sup> Another way to screen for PJS is by genetic testing. Identifying the PJS-mutation in the STK11 gene is very accurate, with a detection rate of more than 90%.<sup>25</sup>

A sizable percentage of patients suffer from short bowel syndrome as a consequence of the repeated bowel resections. Recently, intraoperative endoscopy and endoscopic polypectomy, rather than segmental resection of the bowel, have been recommended. Periodic endoscopic screenings are advocated every 2 years. The new mouth to anus (M2A) capsule endoscopy will probably become the most useful screening tool in the near future.<sup>5</sup>

#### Conclusion:

In our study the frequency of PJS polyps was very low but these patients should be regularly and closely monitored because of the risk of cancer and to reduce the number of laparotomies. Surveillance and planned comprehensive care may reduce the morbidity of the condition.

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